

Clinical Laboratory Improvement Advisory Committee

August 12, 1993

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Record of Attendance

The Clinical Laboratory Improvement Advisory Committee (CLIAC) met at the Centers for Disease Control and Prevention (CDC), Auditorium A, in Atlanta, Georgia on August 12, 1993. Those in attendance are listed below:

Committee Members

Dr. J. Scott Abercrombie
Dr. Paul Bachner
Ms. Virginia Charles
Dr. S. Raymond Gambino
Ms. Lynne Garcia
Dr. Stanley Inhorn
Ms. Sandra Johnson
Dr. J. Stephen Kroger
Dr. George Lundberg
Dr. Kenneth Matthews
Dr. Brenda McCurdy
Dr. Robert Nakamura
Dr. Wendell O'Neal
Dr. Robert Pierre
Dr. Dorothy Rosenthal
Dr. Morton Schwartz
Dr. Ronald Zabransky

Ex Officio Members

Dr. Carlyn Collins, CDC
Ms. Jan Ohrmundt, FDA
(for Dr. Steve Gutman)
Ms. Judith Yost, HCFA

Executive Secretary

Dr. Edward Baker

Centers for Disease Control and Prevention

Ms. Nancy Anderson
Ms. Rosemary Bakes-Martin
Ms. Louise Barden
Dr. Joe Boone
Ms. Genoria Bridgeman
Ms. Cheryl Coble
Ms. Carol Cook
Ms. Crystal Frazier
Ms. Clio Friedewald
Mr. Edwin Holmes
Dr. John Ridderhof
Ms. Eunice Rosner
Ms. Elva Smith
Ms. Julie Wasil
Ms. Rhonda Whalen
Mr. Mark White

Clinical Laboratory Improvement Advisory Committee

The Secretary of Health and Human Services is authorized under Section 353 of the Public Health Service Act, as amended, to establish standards to assure consistent, accurate, and reliable test results by all clinical laboratories in the United States. The Secretary is authorized under Section 222 to establish advisory committees.

The Clinical Laboratory Improvement Advisory Committee (CLIAC) was chartered in February 1992 to provide scientific and technical advice and guidance to the Secretary and the Assistant Secretary for Health regarding the need for, and the nature of, revisions to the standards under which clinical laboratories are regulated; the impact on medical and laboratory practice of proposed revisions to the standards; and the modification of the standards to accommodate technological advances.

The committee consists of 20 members, including the Chair. Members are selected by the Secretary from authorities knowledgeable in the fields of microbiology, immunology, chemistry, hematology, pathology, and representatives of medical technology, public health, clinical practice, and consumers. In addition, CLIAC includes three ex officio members, or designees: the Director, Centers for Disease Control and Prevention; the Commissioner, Food and Drug Administration; and the Administrator, Health Care Financing Administration.

Due to the diversity of its membership, CLIAC is at times divided in the guidance and advice it offers to the Secretary. Even when all CLIAC members agree on a specific recommendation, the Secretary may not follow their advice due to other overriding concerns. Thus, while some of the actions recommended by CLIAC may eventually result in changes to the law, the reader should not infer that all of the advisory committee's recommendations will be automatically accepted and acted upon by the Secretary.

Introduction to the CLIAC Meeting

August 12, 1993

The CLIAC members were welcomed to the meeting by Executive Secretary Baker and Chairman Schwartz.

Dr. Baker informed the committee of the most recent compilation of test categorizations published in the Federal Register dated July 26, 1993. He thanked the committee for all of their previous recommendations and indicated that their insights would be needed in establishing the revised final rule.

Executive Summary Report of the May 26-27, 1993 CLIAC Meeting

Committee Chairman Schwartz provided a summary of the issues, discussions, and recommendations of the previous CLIAC meeting, held on May 26-27, 1993. The committee recommended that the minutes of that meeting be accepted as recorded.

Note: The name of Dr. J. Scott Abercrombie was inadvertently omitted from the record of attendance for the May 26-27, 1993 meeting.

The Issues

This portion of the meeting included presentations, subcommittee reports, and discussions focusing on criteria for waiver, the addition of specialty subcategories to the physician-performed microscopy category, a proposed robust test category and cytology proficiency testing. These topics arose during previous discussions of issues that were selected from comments received in response to the *Final Rule* published in the Federal Register dated February 28, 1992 and the *Technical Correction* published in the Federal Register dated January 19, 1993.

For each issue, CDC provided a technical overview which included background information and one or more proposals.

The public was invited to address the committee during the afternoon session on August 12, 1993. Their comments and presentation materials are also incorporated into this summary.

Subcommittee on Test Categorization: Report on Criteria for Waiver Presentation

I. Presentation

The report was made by Subcommittee Chairman, Dr. Stephen Kroger.

The subcommittee made the following recommendations:

- Define the criteria for waiver utilizing the language stated in the Act:

"Simple laboratory tests and examinations which have an insignificant risk of an erroneous result."
- Discuss whether tests cleared for home use by FDA should be considered waived.
- Eliminate "risk of harm" from the CDC proposed criteria for waiver.

II. Issue

What operational definition should the committee use for criteria for waiver?

III. Committee Discussion

Dr. Kroger was asked why the phrase "as determined by the Secretary" which was stated in the Act, had been excluded from the recommendation. He indicated that the subcommittee was merely trying to provide a clear statement of the criteria and that there was no intention to exclude the Secretary. Dr. Kroger then briefed the committee on the FDA clearance processes. There was some discussion of how "insignificant risk" would be determined and if it should include clinical risk. Dr. Lundberg asked that the record show he was uncomfortable with the committee attempting to define insignificant clinical risk. Chairman Schwartz suggested that the committee hear the remainder of the subcommittee report and the CDC presentation before resuming this discussion. Ms. Charles was very concerned about the possibility of the glucometer remaining in the waived category and the automatic waiver of any tests cleared for home use. The committee recommended that all tests, including any cleared by FDA for home use, be required to meet the proposed CDC protocol (Addendum B) for implementing the criterion of waiver.

Criteria of Waiver

I. Presentation

(See Addendum A)

The technical presentation was made by Ms. Rosemary Bakes-Martin, Health Scientist, Activity Chief for Quality Control and Test Categorization, Laboratory Practice Standards Branch, Division of Laboratory Systems, PHPPPO, CDC.

II. Issue

The CDC presented a proposal for applying the criteria for waiver.

III. Committee Discussion

Chairman Schwartz thanked CDC for a "remarkably detailed proposal." The committee was concerned with the possibility of matrix effects when using stabilized sample materials of a known value to establish accuracy. The CDC responded that it would consider data provided by the manufacturer showing a matrix effect between referenced fresh serum and the stabilized material. Dr. Gambino stated that he had reviewed the CDC proposal in detail and while his initial reaction had been that the protocol was too stringent, he feels these tests must be exceptionally robust, and that the CDC protocol is appropriate. He stated the manufacturers should be given a standard to work toward and that he believes these standards are attainable. Dr. Rosenthal and Dr. Lundberg suggested revising the criterion proposed by the subcommittee to state: "Simple laboratory tests and examinations which have an insignificant risk of producing an erroneous laboratory test result." The committee recommended that CDC use this as the criterion for waiver. Dr. Bachner asked why the proposed performance characteristics seemed to distinguish systematic from constant and proportional error. Ms. Bakes-Martin indicated that systematic error would be assessed first to determine overall acceptability. Constant and proportional error, which are components of systematic error, would then be evaluated individually to determine their acceptability. Dr. O'Neal asked if Option B under the Phase I proposal for assessing quantitative tests was necessary because Tonk's formula was too "tight." The CDC responded that Tonk's formula was too restrictive for certain tests such as therapeutic drugs.

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III. Committee Discussion (continued)

Dr. O'Neal pointed out that matrix effects could be a problem when comparing test(s) to a reference method in Phase II. Dr. Bachner indicated he was uncomfortable moving forward with the potential for multi-analyte devices in the waived category. Other committee members indicated they would support the inclusion of multi-analyte devices. The committee indicated it wished to consider the implications of this issue further and resume the discussion at a future meeting. The committee agreed with the other provisions of the CDC proposals. Dr. Kroger complimented CDC on its approach to developing these criteria and the detail that had been added since the subcommittee meeting.

IV. Considerations for CDC

The committee recommended that CDC consider the following:

- Use "Simple laboratory tests and examinations which have an insignificant risk of producing an erroneous laboratory test result" as the criterion for waiver.
- Eliminate "risk of harm" as a criteria for waiver.
- Require that all tests, including any cleared by FDA for home use, meet the proposed CDC protocol (Addendum B) in order to be waived.
- Temporarily remove the multi-analyte criteria restricting these devices to single sample use with no independent selection of analytes and consider the two following points:
 - Removal of the criteria may serve to promote the development of simple, useful, multi-analyte technology.
 - Inclusion of the criteria may result in the proliferation of multi-analyte instruments incorporating unnecessary tests that must be run as part of each panel.

The committee otherwise endorsed the CDC protocol for implementing the criterion of waiver (Addendum B).

**Subcommittee on Test Categorization Report on
Physician-Performed Microscopy Specialty Subcategories**

I. Presentation

The report was made by Subcommittee Chairman, Dr. Stephen Kroger.

The Subcommittee on Test Categorization recommended acceptance of PPM specialty subcategories.

II. Issue

Should specialty subcategories be added to the PPM category?

III. Committee Discussion

The committee deferred discussion until the CDC presentation had been made.

Physician-Performed Microscopy Specialty Subcategories

I. Presentation

(See Addendum B)

The technical presentation was made by Ms. Nancy Anderson, Health Scientist, Division of Laboratory Standards, LPSB, PHPPO, CDC.

II. Issue

CDC presented a proposal to add specialty subcategories to the physician-performed microscopy category.

III. Committee Discussion

The committee discussed the use of the terms "board certified" and "board eligible." Dr. Matthews indicated that "board eligible" would be an appropriate term under certain circumstances. Several committee members were concerned about defining competency standards for physicians in general. Dr. Collins indicated that CDC was sympathetic to these concerns, but as of yet had been unable to devise a feasible alternative. Dr. Bachner indicated that he did not believe either term was appropriate and that the determination should be based on the technology of the procedures. Dr. Lundberg stated he believed this type of process equated to federal licensure by procedure, was inappropriate, and ignored the states right to license physicians. Dr. Kroger agreed with this position and suggested that the physician be required to provide proof of his or her competency. Chairman Schwartz then attempted to refocus the discussion and determine the - committees position. The committee voted to forward a recommendation not to utilize board certification as the standard for competency. Ms. Yost and Dr. McCurdy opposed the recommendation and supported the CDC proposal. Dr. Schwartz then asked the committee if they otherwise supported the CDC proposals. Dr. Gambino proposed the addition of tests to the PPM category in general, but was opposed to creating specialty subcategories. Dr. Lundberg supported Dr. Gambino's proposal. Ms. Johnson reminded the committee that it had previously recommended that mid-level practitioners be permitted to perform the tests in the PPM category. Dr. Bachner restated Dr. Gambino's proposal specifying that these tests would be performed by the physician only and would not be performed by mid-level practitioners. Dr. Rosenthal suggested elimination of specialty orientation and recommended the nature of the tests be the primary consideration. Dr. Kroger suggested the addition of one subcategory to the PPM category and that this subcategory be limited to physicians only.

III. Committee Discussion (continued)

Dr. Gambino indicated that the gram stain is badly needed by physicians in the field and that the committee should encourage the manufacturers to perfect a simplified gram stain. Dr. McCurdy moved that the committee recommend that gram stains be excluded from the PPM category. The motion was seconded. Dr. Kroger spoke against the motion, indicating he believed that the physicians would recognize their own professional limitations. Dr. O'Neal asked why performing the gram stain as part of a regulated category would be a burden. Dr. McCurdy again moved that the committee recommend the gram stain be excluded from the PPM category. The motion was carried with Drs. Gambino, Kroger, and Matthews opposed. Chairman Schwartz then called for a motion on the Tzank preparation. He received a motion that the committee recommend exclusion of the Tzank preparation from the PPM category. The motion was carried with Dr. Kroger, Dr. Lundberg, and Dr. Matthews opposing. Dr. Pierre moved to recommend exclusion of the V;BC differential from the PPM category. The motion was carried with Dr. Lundberg opposed. The committee then reached a general consensus to recommend the inclusion of qualitative semen analysis in the PPM category.

IV. Considerations for CDC

- The committee recommended not to utilize board certification as the standard of competency for the PPM category.
- The committee recommended not to accept PPM specialty subcategories. Instead, it recommended that a limited number of tests be added to the PPM category including:
 - Fecal leukocyte examination
 - Wet mount examination of prostatic secretion
 - Qualitative semen analysis
- The committee was divided on the issue of excluding the following tests from the PPM category:
 - Histodermatology slides
 - Quantitative semen analysis
 - Polarization of synovial fluid
 - Tzank preparations
 - Gram Stain
 - WBC differential

Subcommittee on Test Categorization

Report on the Proposed Robust Test Category

Dr. Kroger briefed the committee on the CDC presentation to the Subcommittee on Test Categorization. He then indicated that CDC was continuing work on this proposal and would make a presentation to the full committee at a future meeting.

Cytology Proficiency Testing

I. Presentation

(See Addendum C)

The technical presentation was made by Dr. Carlyn Collins, M.D., M.P.H., Director, Division of Laboratory Systems, PHPPPO, CDC.

II. Issue

Dr. Collins reported on the alternative strategies for providing a national proficiency testing (PT) program. She reminded the committee that no bids were obtained to provide a PT program by the January 1, 1994 implementation deadline.

The law requires:

- Periodic ... evaluation of the proficiency of individuals.
- Announced and unannounced on-site testing.
- To the extent practicable, the testing should take place under normal working conditions.

The regulations require:

- PT for each individual, each year, administered on-site.
- 10 glass slides with a passing score of 90 percent.
- All cytology laboratories must enroll in a national PT program by January 1, 1994.

Alternatives proposed to CDC

- Test the laboratory rather than individuals.
- Utilize mailed glass slides.
- Utilize a combination of color transparencies and glass slides.
- Develop computer imaging system for testing.

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Cytology Proficiency Testing

Advantages of computer-based systems for cytology PT

- Standardization
- Fewer slides required
- More options for administering tests
- Long-term cost is probably lower

Issues concerning computer-based systems for cytology PT

- Dependent on the current status of technology
- Difficult to duplicate normal working conditions
- Acceptability to the cytology community

Dr. Collins announced an upcoming scientific cytology meeting on November 16-17, 1993.

III. Committee Discussion

The committee asked Dr. Collins if the regulatory requirement to save slides limited the ability to obtain slides for PT. She indicated it was indeed a major part of the problem. Dr. Rosenthal noted that huge numbers of slides must be screened in order to obtain the slides which are appropriate for PT. Chairman Schwartz stated that he hoped the CLIAC Subcommittee on Cytology would be invited to the scientific meeting in November. Dr. Rosenthal questioned the 1/2 slide rule for the automated preparation of gynecologic slides, which allows an individual to screen as many as 200 slides per shift. Dr. Collins reviewed the history of this regulation. Dr. Gambino also questioned this regulation and requested additional data be provided. Chairman Schwartz asked CDC to research the performance data and present their findings at the December 1993 CLIAC meeting.

Public Comments

Stanley Lapitas, President of Cytec, made a public comment addressing indirect versus direct QC methods. He also addressed slide workload limits. He recommended utilizing cell suspensions to make slides for PT testing. He also suggested that an alternative to the requirement to rescreen ten percent of the slides, would be to utilize ten percent seeded suspensions which would provide an ongoing PT process.

Richard Dubois, President of the Infectious Disease Society of Georgia, was generally perplexed by the complexity categorization of the gram stain.

Bryan Jansen representing the American Academy of Family Physicians (AAFP), seconded the remarks made by Dr. Dubois. He thanked Chairman Schwartz for recognizing that family physicians were being affected by these regulations and indicated that he would appreciate anything CLIAC could do reduce the burden of CLIA on family physicians.

Dr. Basil Doumas, professor of Pathology at the Medical College of Wisconsin and past president of American Association for Clinical Chemistry (AACC), made a personal statement addressing the use of "board certified" as it applies to the clinical consultant personnel standards. He indicated that this provision may disenfranchise hundreds of laboratory directors who can no longer serve as clinical consultants. He suggested that those individuals with extensive experience in directing a laboratory should be deemed qualified or grandfathered.

Nanci Highsmith of Wampole Laboratories asked the committee how long the moratorium on additions to the waived category would continue, and if the products currently enjoying waived status would be removed until such time as the moratorium is lifted.

Carol Stevens from the NC Office of Rural Health addressed the committee concerning rural health issues and the ability of physicians in general to perform microscopy.

Closing Remarks

Dr. Boone indicated that CDC will send the Federal Register Notices to the committee members along with occasional updates.

Dr. Schwartz reminded the committee that the next meeting would be December 14-15, 1993.

I certify that this summary report of the August 12, 1993 meeting of the Clinical Laboratory Improvement Advisory Committee is an accurate and correct representation of the meeting.

Morton K. Schwartz, Ph.D.
Chairman